Screening and Management of Maternal HIV Infection

Implications for Mother and Infant

Produced by
Northwest Regional Perinatal Program
Department of Obstetrics and Gynecology
Division of Perinatal Medicine
University of Washington
And
Department of Pediatrics
Division of Neonatology
Children's Hospital and Regional Medical Center
University of Washington
Seattle, Washington
And Washington State Department of Health
Olympia, Washington

Revised Edition, 2003

For persons with disabilities, this document is available on request in other formats. Please call 1-800-525-0127.

University of Washington School of Medicine
Department of Obstetrics and Gynecology
Division of Perinatal Medicine
Box 356460
Seattle, WA 98195-6460
(206) 221-7362

Screening and Management of Maternal HIV Infection: Implications for Mother and Infant

(Revised Edition, 2003)

editors

Jane E Hitti, MD, MPH (2003)
Deborah C Goldman, ARNP, MPH (2000)
Nancy O'Brien-Abel, MN, RNC (1998)

contributing authors (1998)

Sylvia J Berry, ARNP
D Heather Watts, MD
Ann J Melvin, MD

preface

Jane E. Hitti, MD, MPH

layout and design

Jan Hamanishi (1998/2000)
Rebecca Ross (2003)

Information about HIV medications for pregnant and postpartum women and newborns outdates quickly. For current recommendations, contact:

- An infectious disease specialist knowledgeable about perinatal HIV
- Go to http://www.aidsinfo.nih.gov/
- Call the CDC Hotline 1-800-342-AIDS
- Call Northwest Family Center 206-731-5100

2003 Editors

Jane E Hitti, MD, MPH
Assistant Professor, Department of Obstetrics & Gynecology
Adjunct Assistant Professor, Department of Epidemiology
University of Washington School of Medicine, and
Obstetric Medical Director
Seattle-King County Department of Public Health

Ann J Melvin, MD
Assistant Professor, Department of Pediatrics
Division of Infectious Diseases
Children's Hospital and Regional Medical Center
University of Washington

2000 Editor:

Deborah C Goldman, ARNP, MPH
Women's Health and Adult Primary Care Nurse Practitioner
Northwest Family Center
Harborview Medical Center
University of Washington

1998 Editor:

Nancy O'Brien-Abel, MN, RNC
Perinatal Clinical Nurse Specialist
Northwest Regional Perinatal Program
Department of Obstetrics and Gynecology
Division of Perinatal Medicine
University of Washington

1998 Contributing Authors:

Sylvia J Berry, ARNP
Women's Healthcare Nurse Practitioner
Department of Obstetrics and Gynecology
Divisions of Perinatal Medicine & Women's Health
University of Washington

D Heather Watts, MD
Associate Professor
Department of Obstetrics and Gynecology
Division of Perinatal Medicine
University of Washington, and
Obstetric Medical Director
Seattle-King County Department of Public Health

Ann J Melvin, MD
Assistant Professor, Department of Pediatrics
Division of Infectious Diseases
Children's Hospital and Regional Medical Center
University of Washington

Reviewers:

Zane A Brown, MD (1998)
Professor, Department of Obstetrics & Gynecology
Division of Perinatal Medicine
University of Washington

Joan A Dragavon, MLM (1998/2000)
Clinical Laboratory Supervisor, Retrovirus Lab
Department of Laboratory Medicine
Division of Virology
University of Washington

Reviewers:

Lisa M Frenkel, MD (1998)
Associate Professor, Department of Pediatrics
Division of Infectious Diseases
Children's Hospital and Regional Medical Center
University of Washington

Steven G Gabbe, MD (1998)
Professor and Chair, Department of Obstetrics & Gynecology
University of Washington

Christine A Gleason, MD (1998)
Professor, Department of Pediatrics
Director, Division of Neonatology
University of Washington

Amy Manchester Harris, MPA (2000)
Education Coordinator, HIV Prevention & Education Services
Washington State Department of Health, Olympia, WA

Jane E Hitti, MD, MPH (2000/2003)
Assistant Professor, Department of Obstetrics & Gynecology
Adjunct Assistant Professor, Department of Epidemiology
University of Washington School of Medicine, and
Obstetric Medical Director
Seattle-King County Department of Public Health

J Craig Jackson, MD (1998)
Associate Professor, Dept of Pediatrics, Division of Neonatology
University of Washington, and
Director, Infant Intensive Care Unit
Children's Hospital and Regional Medical Center

Terrie M Lockridge, MS, RNC (1998/2000)
Neonatal Clinical Nurse Specialist, NW Regional Perinatal Prgrm
Department of Pediatrics, Division of Neonatology
Children's Hospital and Regional Medical Center
University of Washington

Ann J Melvin, MD (1998/2000/2003)
Assistant Professor, Department of Pediatrics
Division of Infectious Diseases
Children's Hospital and Regional Medical Center
University of Washington

Kathey M Mohan, MN, ARNP (1998/2000)
Pediatric Nurse Practitioner, Department of Pediatrics
Division of Infectious Diseases
Children's Hospital and Regional Medical Center
University of Washington

Nancy O'Brien-Abel, MN, RNC (1998/2000/2003)
Perinatal Clinical Nurse Specialist, NW Regional Perinatal Prgrm
Department of Obstetrics & Gynecology
Division of Perinatal Medicine
University of Washington

Reviewers:

Mary Jo O'Hara, MSN, ARNP (1998)
Pediatric Nurse Practitioner, Department of Pediatrics
Division of Infectious Diseases
Children's Hospital and Regional Medical Center

Polly Taylor, CNM, MPH, ARNP (2000/2003)
Public Health Nurse Consultant, Maternal and Infant Health
Washington State Department of Health
Olympia, Washington

Jeanette Zaichkin, MN, RNC (2000/2003)
Public Health Nurse Consultant, Maternal and Infant Health
Washington State Department of Health
Olympia, Washington

John Peppert (2003)
Manager, HIV/AIDS Prevention and Education Services
Washington State Department of Health
Olympia, Washington

Table of Contents

Preface 9
HIV Testing During Pregnancy 10
HIV Counseling During Pregnancy
Pre-test Counseling and Risk Reduction 12
HIV Diagnostic Tests 13
Post-test Counseling:
Negative Results 15
Indeterminate Results 16
Positive Results 17
Partner Notification 18
Perinatal HIV Transmission
Risk 18
Timing 19
Consultation and Referral of HIV-Infected Pregnant Women 19
Laboratory Tests for Positive Women
Laboratory Monitors of HIV Infection 20
Laboratory Tests for HIV-Infected Pregnant Women 21
Laboratory Tests Measuring HIV Disease Progression 21
Schedule of Laboratory Tests 22
CDC HIV Classification of Disease and Reporting 23
Medications/Treatment During Pregnancy, Labor, and Delivery
Medications Available 24
Treatment Recommendations 25
Antiretroviral Pregnancy Registry 27
History and Physical of HIV-Infected Pregnant Women 27
Medication During Labor 28
Cesarean Birth 30
Avoiding Risk of Transmission 31
Postpartum Management
Treatment 31
Postpartum Care 32
Contraception 32
Patient Education 33
The HIV-Exposed Infant
Laboratory Tests 33
Medications and Treatment 34
Testing and Consultation 35
Schedule of Testing 35
Diagnosis of HIV 35
Appendix A— Resource Directory 36
Appendix B—Washington State Local Health Jurisdictions 39
Appendix C—Free Regional and National Telephone Consultation 41
Appendix D—Websites 42
References 43

Preface

The past decade has brought tremendous advances in the prevention of HIV transmission from mother to infant. Before AZT therapy was available, approximately 25–30% of HIV-positive women in the U.S. transmitted HIV to their infants. With AZT alone, the rate of infection fell to 5–8%. Most recently, studies have shown that HIV-positive pregnant women who have a good response to combination HIV therapy (viral load <1000 copies/ml) have a 2% rate of transmitting HIV to their infants. This same low rate can also be achieved for women with higher viral loads by performing a Cesarean delivery prior to the onset of labor or ruptured membranes.

As health care providers for the pregnant woman, we have an obligation to care for both the mother and her fetus. Prevention of infant HIV transmission is a critical aspect of HIV care for the pregnant woman. However, we must also be certain that HIV treatment in pregnancy does not adversely affect a woman's health or compromise her choices for treatment in the future. Current treatment guidelines recommend offering comprehensive antiretroviral therapy to all HIV-positive pregnant women, even if they do not meet criteria for treatment outside of pregnancy. Optimizing maternal health will also increase chances of having a healthy infant, since maternal HIV viral load is the most important predictor of infant HIV infection.

With the current spectrum of anti-HIV drugs, the outlook for adults with HIV infection has brightened considerably. Compared to 8 years ago, HIV-positive women can now expect to feel better and live longer. For many HIV-positive women, having children is an important part of their life plan. The approach to these women should be similar to that for women with other chronic illnesses, such as diabetes or hypertension, who become pregnant.

Prevention remains the key to eradicating HIV disease. By screening for HIV in pregnancy, we can identify HIV-infected women and greatly decrease the risk of perinatal HIV transmission while improving maternal health. In addition, HIV testing in pregnancy provides the opportunity to counsel HIV-negative women about reducing their risk of HIV acquisition. The information in this handbook is intended to help us all with the continuing effort to prevent HIV infection in women and infants.

Jane E Hitti, MD, MPH

Assistant Professor, Department of Obstetrics and Gynecology

Adjunct Assistant Professor, Department of Epidemiology

University of Washington School of Medicine, and

Obstetric Medical Director, Seattle-King County Department of Public Health

HIV Testing During Pregnancy

Should all women be tested for human immunodeficiency virus (HIV) during their pregnancy?

All pregnant women should be tested for HIV prior to pregnancy or as early in pregnancy as possible. Dramatic declines in reported pediatric AIDS cases have been observed due to major advances in the treatment of HIV infection and prevention of perinatal transmission.

However, screening pregnant women in the U.S. has been far from universal, and infected babies continue to be born to undiagnosed infected women. In 1998 the Institute of Medicine (IOM) completed a study of interventions that would be helpful to further reduce the rate of perinatal HIV infection in the U.S. They have recommended a national policy of universal testing, with patient notification, as a routine component of prenatal care.

In May of 1999 the American College of Obstetricians and Gynecologists (ACOG) and the American Academy of Pediatrics (AAP) issued a joint statement on HIV screening supporting the IOM recommendation.

Principles of universal HIV testing for pregnant women:

- HIV test is integrated into a standard battery of prenatal tests
- Pregnant women are informed that the HIV test is being conducted and would have the right to refuse it
- Universal testing applies to all pregnant women regardless of risk factors or prevalence rates where they live

The Washington State Board of Health adopted revised rules for AIDS counseling for pregnant women. Effective July 6, 2002, these new rules were designed to reduce barriers to routine HIV testing of pregnant women, consistent with the recommendations of the Centers for Disease Control and Prevention, the Institute of Medicine, the American College of Obstetricians and Gynecologists, and other national and state organizations.

In part, the amended rules require health care providers to:

1. Encourage all pregnant women to have a test for HIV, regardless of identified risk.
2. Obtain the verbal or written consent of the pregnant woman prior to testing. The consent may be part of the general consent for other tests provided that the woman is informed a test for HIV is included. If the test is refused, refusal must be documented in the patient's medical record.
3. Provide information, either verbally or in writing, addressing:

- All pregnant women are recommended to have an HIV test;
- HIV is the cause of AIDS and how HIV is transmitted;
- A woman may be at risk for HIV infection, and not know it;
- The efficacy of treatments to reduce vertical transmission;
- Anonymous testing is available, and why confidential testing is recommended;
- The need to report HIV infection;
- Public funds are available to assist eligible infected women to receive HIV care; and
- Women who decline testing will not be denied care for themselves or their infants.

4. Provide counseling to those women who identify a behavioral risk for HIV, based on the risk assessment

The Washington State Department of Health has developed a patient brochure that meets the requirement to provide certain information to the pregnant woman. For copies, contact Teri Hintz at (360) 236-3425 or by email at teri.hintz@doh.wa.gov.

Risk factors for HIV infection in pregnant women include:

- ► Injection drug use (IDU)
- ► Multiple sex partners
- ► History of sexually transmitted diseases
- ► Blood transfusions or artificial insemination prior to 1985
- ► Sexual partners who are (current or past):
  - HIV infected
  - Injection Drug Users
  - Men who have sex with other men
  - Having unprotected sex with multiple partners
  - Diagnosed or have history of sexually transmitted diseases, and/or
  - Recipients of blood transfusions prior to 1985

In Washington State, for almost two-thirds of the HIV-infected women, heterosexual sex was identified as the exposure risk. Sex partners of three-quarters of these women were identified as HIV-infected or at high risk of HIV infection, although infection status or risk behavior of these partners may not have been known to these women until they were diagnosed with HIV.

Data has shown that nationwide, even in areas of high HIV prevalence, half of the HIV-infected women were not aware of having HIV risk factors. The following cases are illustrative.

Case #1: A 32-year-old white woman with 3 children from a previous marriage acquired a new partner. Neither she nor her new partner had any HIV risk factors. He was HIV negative. She had a lifetime history of less than 5 heterosexual partners, none of whom, to her knowledge, exhibited high risk behavior. During the fourth pregnancy, she tested HIV positive and received antiviral chemotherapy. This child has remained HIV negative and is currently 1 year of age. Unfortunately, her other children, ages 6, 4 and 2 are HIV positive. Too late, she learned that her former husband was HIV positive. She had been unaware of his risk taking behaviors. Had she been tested during previous pregnancies, she may have known her HIV status early enough to possibly prevent her children from becoming infected.

Case #2: A 27-year-old single woman was a regular blood donor. The last time she donated (before her pregnancy), she was informed that she was HIV positive. She had no risk factors other than approximately 10 lifetime sex partners, none of whom, to her knowledge, exhibited high-risk behavior. Too late, she learned that one of her partners was HIV positive. He was aware of his HIV status during their relationship, but did not reveal this information to her.

HIV Counseling During Pregnancy

What are the most important points to cover in HIV pre-test counseling for pregnant women?

1. All pregnant women must be offered and encouraged to have HIV testing. Having sex is the only identified risk factor for more than 60% of HIV-infected women in Washington State. Women often learn of their positive HIV status when they are offered and accept testing for HIV during pregnancy.
2. Test results are confidential and filed in the patient's chart. Access to test results is limited to medical personnel, by written consent of patient, or as specifically allowed by law (e.g., case reporting to the health department, filing insurance claims).
3. Health care providers offering HIV testing in Washington State are required to make the patient aware of options for either confidential or anonymous testing. As required by state law, the pregnant woman must receive information, either verbally or in writing, addressing the eight points listed on page 14. Anonymous testing is available through most health jurisdictions and some other community organizations (e.g., Planned Parenthood clinics).
4. Test results:

► Confirmed positive antibody test indicates infection with HIV

► Indeterminate test means repeat testing is needed to differentiate between a recent infection with HIV vs. cross-reacting antibodies

► Negative test means no HIV infection or that infection happened too recently to reliably detect antibodies (within the past month or, in rare cases, longer)

► HIV infection is now a reportable disease in Washington State. Reporting is done only after the provider has seen the patient and had a chance to answer questions about the "hows and whys" of reporting. Call your local health department for more detailed information about HIV reporting.

5. RISK REDUCTION/SAFER SEX BEHAVIORS include:

► Practicing abstinence from sex and drugs

► Having a single, long-term, mutually-monogamous relationship in which neither partner is infected

► Safer sex practices:

- Limiting number of sex partners
- Using latex condoms/barriers consistently and with water-based lubricants rather than oil-based, as oil-based lubricants damage condoms

► Not reusing (sharing) drug injecting equipment (needles/syringes), or else rinsing equipment well with water to get all blood out, filling with bleach and letting sit for a full 30 seconds, then rinsing again with water

6. Benefits of being tested:

► Early treatment is important for maintaining a woman's health

► Treatment is available to reduce HIV transmission from mother to fetus/infant

- Probability of transmission from an untreated mother to fetus/infant is about 25%
- With AZT treatment, risk of transmission is reduced to 5–8%

- With highly active antiretroviral treatment (HAART) consisting of 3 or more drugs, and suppression of plasma HIV to a low level (viral load <1000 copies /ml), transmission is reduced to about 2%
- With a viral load of >1000 copies, a scheduled cesarean delivery prior to the onset of labor or ruptured membranes may also reduce the risk of transmission to about 2%

► Knowing results allows for informed reproductive decision-making

7. Risks of being tested:

► Test and results can be emotionally upsetting

► Waiting for test results can be difficult

► Sometimes the test cannot show present status of infection. Antibody testing can be done as early as one month, although it may take up to three months for a test to show positive for antibodies. In rare cases, it may take as long as six months.

► Concerns about consequences of a positive test (e.g., partner reaction or questions of insurability)

8. Testing options:

► Test now

► Get tested at an anonymous site

- Patient's blood is assigned a code
- There is no record of the test

► Decline testing. Ensure the woman understands the reason for testing.

► Think it over

- Women can request an HIV test at any time during their prenatal care

9. Provide time for women to have their questions answered

10. Documentation:

- Obtain the verbal or written consent of the pregnant woman prior to testing. The consent may be part of the general consent for other tests provided that the woman is informed a test for HIV is included. If the test is refused, refusal must be documented in the patient's medical record.

Note: *All health care providers should assess the psychological status of a person before testing. If the individual is at high risk of a positive HIV antibody test result and expresses an intent to harm herself or others in response to a positive test, the provider should defer testing and assist the patient in developing a more functional coping strategy prior to testing. This may include a better understanding of the meaning of a positive test result, transmission precautions, and identification of local support systems.*

What are the laboratory HIV diagnostic tests?

► Screening Antibody Test: Enzyme Immunoassay (EIA or ELISA)*

- Sensitivity and specificity >99%
- Positive predictive value of a reactive EIA ranges from 20% to over 95%, with lower values in low HIV prevalence populations
  - ◊ Based on sensitivity of the EIA, as well as prevalence of HIV in the population tested

- Specificity of <100% necessitates use of a confirmatory assay to ensure that the antibody reaction is specific for HIV

  Test Interpretation: Reactive or Non-Reactive

  *This test alone cannot be used to provide a positive result as per Washington State law and CDC (Centers for Disease Control and Prevention) guidelines.

► Confirmatory Antibody Test: HIV Western blot

- Most commonly used confirmatory test
- Detects serum antibodies directed against specific HIV-1 proteins of various parts of the virus:
  - ◊ Core protein (gag) (p17/18, p24, p55)
  - ◊ Polymerase protein (pol) (p31, p51, p66)
  - ◊ Envelope protein (env) (gp41, gp120/160)
- The CDC has defined a positive HIV-1 Western blot as the presence of antibody bands against at least two or more of the following HIV-1 proteins:
  - ◊ p24
  - ◊ gp41
  - ◊ gp120/160

Test Interpretation: Positive, Negative, or Indeterminate

► Indeterminate Western blot

- A Western blot is interpreted as indeterminate when one or more of the antibodies directed against specific HIV-1 proteins are present, but CDC criteria for a positive Western blot, as defined above, are not met (e.g., the patient has p24 and p17/18 bands, but not gp41 or gp120/160)
- Among blood donors, approximately 10 out of every 10,000 individuals (0.1%) without known risk factors for HIV-1 will have a repeatedly reactive HIV-1 EIA test
  - ◊ Among these 10 low-risk individuals, 8 will have a negative and 2 will have an indeterminate Western blot
- Overall risk of seroconversion among a population including both low- and high-risk persons with an indeterminate Western blot is approximately 3.0%
  - ◊ Risk of seroconversion is determined by an individual's risk history and band(s) present on the Western blot
  - ◊ With high-risk behavior and a p24 band, risk of seroconversion is 18%
  - ◊ p24 is the most common band associated with possible early seroconversion; it is also a common "non-specific" indeterminate result that does not indicate seroconversion
  - ◊ With no identifiable risk and an indeterminate Western blot, seroconversion is rare
- Confirmation or exclusion of HIV infection should be made on the basis of the patient's antibody test results, as well as consideration of her
  - ◊ Medical and behavioral history
  - ◊ Additional virologic and immunologic tests (i.e., HIV-1 DNA PCR, HIV-1 viral load, or PBMC culture), when performed

- ◊ Partner's HIV status
- ◊ Clinical follow-up
- ◊ See page 16 for follow-up details of an indeterminate Western blot

► Tests for Virus

- HIV antibodies may not be detected for a "window period" of weeks or up to several months following infection window period
- Four tests can detect HIV infection before the appearance of a complete antibody pattern:

1. Nucleic Acid (polymerase chain reaction or PCR)
   - ◊ Qualitative HIV DNA PCR is the recommended PCR test if recent infection is suspected and antibody tests are negative
2. Infectious Virus (mixed lymphocyte culture)
   - ◊ PBMC (cell culture) can be done if PCR is not available or if viral isolate is desired for more detailed studies
3. Viral Load
   - ◊ HIV-1 RNA copies by either bDNA or RT-PCR methodology
   - ◊ Viral load can be used to confirm a reactive EIA with an indeterminate or negative Western blot. The DNA PCR may have false positive results, and should not be the sole basis for diagnosing HIV.
4. Viral Antigen (p24)
   - ◊ Transiently positive, less sensitive, and NOT recommended

► HIV-1 Proviral DNA PCR (HIV DNA PCR)

- Enzymatically amplifies and detects specific DNA sequences
- Highly sensitive and specific methodology used to detect HIV-1 proviral DNA in infected cells
- Blood must be collected in EDTA or ACD tubes (heparin anticoagulant is not acceptable because it interferes with PCR assays)
- Useful to determine infection status of neonates and infants born to HIV-infected women and as a supplement to sort out indeterminate serology results

What are the points to cover in post-test counseling for women with a negative test result?

► Review the purpose of the test and explain that it detects antibodies to HIV

► Give test results

► Because seroconversion generally occurs within a window period of one month and always within six months of infection, a negative result means the woman is probably not infected with HIV unless she has been exposed within the past six months

- If recent exposure is likely, retesting is indicated

► Reiterate risk reduction/safer sex behaviors (as described on page 12)

- ► Assess the woman's psychological well-being and need for support
- ► Assist the woman in identifying needs for further support or referral (e.g., counseling or crisis intervention, screening for other STDs or tuberculosis, substance abuse) and provide as needed
- ► Reinforce the need for retesting if the woman has had recent risks or if new risks occur

What if my patient has an indeterminate result?

- ► Review purpose of the test, explaining that it detects antibodies to HIV
- ► Give test results
- ► Discuss various circumstances that can cause a reactive EIA (other than HIV):
  - Auto immune diseases
  - Liver disease
  - Vaccines (e.g., flu vaccine)
  - Being a multiparous female
  - Rh negative person who has received Rh immunoglobulin
  - Having recently had influenza
  - Having received immunoglobulins
  - Others
- ► Discuss various circumstances that can cause an indeterminate Western blot:
  - Antibodies which cross-react with HIV proteins, but patient does not have HIV
  - Recently infected with HIV and has not yet developed all the usual antibodies (this may take 6 months)
  - Immune system damaged by HIV and no longer making antibodies, which occurs only in advanced stages of HIV/AIDS
  - Infection with HIV-2—rare in the U.S. but common in West Africa
- ► When an indeterminate Western blot result is obtained:
  - **Counsel the woman about the result, emphasizing the low probability of HIV infection if test does not show p24 band and there is no known HIV risk**
  - Explore potential exposures within the past 3 months (needle-sharing, sexual exposure to known HIV-positive or high-risk partner)
  - Recommend partner testing
  - **Repeat EIA and Western blot**
- ► If the repeat test is negative, reassure the woman that she is negative
- ► If the repeat test is indeterminate:
  - Western blot has same isolated reactive band
  - Patient has no risk factors
  - All sexual partners within the last three months are HIV-negative

Then, reassure the woman that she is not HIV-positive. Repeat testing every three months during pregnancy. Explain that she will be excluded from blood donation and that she may have to explain the results to obtain life insurance.

- If the repeat test detects additional bands, then the woman may be seroconverting to HIV and needs aggressive antiretroviral therapy for her own health and to try and reduce perinatal transmission. (See below for counseling for a positive result)
- If the repeat test meets criteria for positive result (see below), the woman has seroconverted
- Consider adding an HIV DNA PCR test to the repeat antibody testing if counseling and risk assessment reveals that the:
  - Woman has had high-risk exposure within the last 3 months, **or**
  - Sexual partners are not available for testing, **or**
  - Woman has symptoms suggestive of an HIV seroconversion illness (e.g., fever, sore throat, malaise, weight loss, disseminated lymph-adenopathy), **or**
  - Woman is in the third trimester of pregnancy
- Counsel the woman to practice risk reduction/safer sex behaviors as described on page 12
- Assess the woman's psychological state and need for support, providing referrals as needed

What do I do if my patient has a positive result?

- Give test results, allowing for the woman to absorb information
  - Assess her psychological well-being and need for support
- Discuss the meaning of seropositive results. A positive test does not mean AIDS; it does mean that the patient is infected and can transmit HIV by sex and needle sharing. Pregnant women can pass HIV to their offspring during pregnancy, at birth, and by breastfeeding.
- Stress to the woman the need to protect others from infection by:
  - Practicing abstinence or safer sex practices as described on page 12
  - Not sharing personal items that might contain blood or vaginal fluids (e.g. razors, toothbrushes, sex toys)
- Assess clinical signs and symptoms, CD4 lymphocyte count, and viral load
  - Discuss treatment options
- Reiterate that treating HIV-infected women with antiretroviral therapy reduces the risk of transmission to their baby from 25% to 5% or less. Scheduled cesarean delivery may also reduce the risk of transmission (see page 30).
- Assist the woman in identifying needs for further support or referral
- When the woman is ready, the following should be addressed:
  - Discuss the relationship between immune system functioning and the development of AIDS
  - If the woman discloses current substance use, discuss benefits of treatment and assist with referrals
  - Stress the need to promote optimal immune system functioning by avoiding cigarettes, non-prescription drugs and excess alcohol, and by eating healthy foods

- Partner Notification
  - ◊ Strongly advise the woman of the importance of notifying sexual and/or needle sharing partners from the period of possible exposure. Federal legislation requires spousal notification if it can be determined that the spouse could have been infected up to 10 years ago. Exposure times depends on the information that the client gives providing evidence of possible exposure to HIV.
  - ◊ Provide assistance to women in notifying partners, including spouses; confirm those partners have been notified and/or
  - ◊ Refer women to the local health department for assistance in notifying partners, and/or
  - ◊ Offer to help refer partners for counseling and testing
  - ◊ Confidentiality must be maintained at all times. A system must be in place to avoid documenting the names of referred partners in the permanent record of the woman being counseled.

If the woman has partners that she is unwilling or unable to notify, the health care provider must report the information and identity of exposed partner(s) to the Washington State Department of Health Office of HIV/ AIDS at 1-800-272-2437. In King County, providers should contact Edith Allen at (206) 205-7192 (Partner Notification Services at Public Health of Seattle and King County).

Perinatal HIV Transmission

If the pregnant woman is HIV positive, what are the chances of infant infection?

► There is a 20–30% risk of infant infection with no treatment. ACTG Study 076 was a randomized, double-blind trial of maternal oral AZT for a mean of 12 weeks antepartum, IV AZT during the intrapartum period, and oral AZT treatment of the infant during the first 6 weeks of life. This study showed a reduction of infant infection from 25% to 8% in the AZT-treated group. Women included in ACTG 076 had CD4 lymphocyte counts above 200/mm^3, and few had previous treatment with zidovudine (AZT, ZDV).

► Subsequent observational studies have confirmed the benefits of AZT treatment during pregnancy, even for women with a CD4 count <200/mm^3 and prior AZT therapy. These studies have shown infant HIV transmission rates of 5–8% among AZT-treated groups.

► Recent observational studies suggest that women on highly active antiretroviral therapy (HAART) consisting of at least three drugs, and with a plasma viral load of <1,000 copies/ml, have about a 2% risk of perinatal HIV transmission. It is not known whether cesarean delivery will further reduce this risk (Mofenson et al., 1999; Garcia et al., 1999).

► Early published data suggest that ZDV plus scheduled cesarean delivery done prior to the onset of labor or rupture of membranes reduces the risk of perinatal transmission to approximately 2%, even in women not on HAART or whose plasma viral load is >1,000 copies/ml (see pages 41–42).

► No combination of therapies can guarantee that a newborn will not become infected.

When are babies infected with HIV?

Antepartum

► 30–50% of infections probably occur before labor

► Risk factors may include:

- Anything that would introduce maternal blood into the amniotic fluid

- ◊ Amniocentesis
- ◊ Fetomaternal hemorrhage
- ◊ Abruptio placenta

- Advanced maternal HIV disease

Intrapartum

► Approximately 50–70% of infected infants acquire the infection at the time of delivery

► Factors that seem to increase the risk of infection include:

- Maternal smoking
- Rupture of membranes (ROM) for >4 hours
- Clinical or histologic chorioamnionitis

► Other concerns include:

- Use of fetal scalp electrode
- Anything that might break the integrity of the skin or mucus membranes of the infant (e.g., forceps/ vacuum extractor)
- Anything that would increase the presence of maternal blood in the birth canal (e.g., early episiotomy)

Postpartum

► Infection occurs by breastfeeding

► Transmission rates vary from 16–35% in different studies

► In the U.S., breastfeeding is **not recommended**

If I identify an HIV-infected pregnant woman, what resources are available for care and/or consultation?

For care and/or consultation for mother and baby, refer to:

Northwest Family Center (NWFC)
Harborview Medical Center, Seattle
206-731-5100 (clinic appointments/medical)
206-731-3066 (case management) or 1-800-462-4965

Pediatric Infectious Disease Group
Children's Hospital and Regional Medical Center, Seattle
206-526-2037

Local, State, and County Health Departments
See Appendix B for list of all Washington State Health Departments

Laboratory Tests for Pregnant Women

What are the commonly used laboratory monitors of HIV infection?

► Lymphocyte subsets (CD4 lymphocyte cell counts)

- CD4 lymphocytes are the major cell type infected by HIV
  - ◊ These cells play a critical role in the immune system
  - ◊ Measured by T-cell subsets, may need to be ordered along with a CBC with differential and platelets
    - – Check with your lab for test requirements
- CD4 lymphocyte counts are measured in three different ways:
  - ◊ Absolute CD4 cell count
  - ◊ CD4 percentage of total lymphocyte count
  - ◊ Ratio of CD4 to CD8 cells
- Clinically, CD4 cell counts are used for three major purposes:
  - ◊ Staging disease, such as assigning a CDC class
  - ◊ Assisting providers in determining when to initiate or change antiretroviral therapy
  - ◊ Determining when to start opportunistic infection prophylaxis

► HIV-1 RNA Quantitation (viral load)

- Integral part of managing patients on antiretroviral therapy
- Patients should be monitored over the course of disease using the same assay each time
  - ◊ Use the same assay consistently, if possible.
- Blood must be collected in EDTA or ACD tubes (heparin anticoagulant is not acceptable because it interferes with PCR assays)
- Two methods commonly available to quantitate plasma HIV-1 RNA:
  1. RT-PCR
     - ◊ Couples a reverse transcriptase (RT) step to change RNA to DNA which is then amplified by PCR to enhance detection and quantitation of specific RNA sequences
     - ◊ Quantitative range of 400–500,000 copies/ml
     - ◊ Ultrasensitive quantitative range of 50–75,000 copies/ml
  2. bDNA (branched chain DNA assay)
     - ◊ Based on “signal amplification” rather than analyte amplification employed by PCR and RT-PCR technologies
     - ◊ Quantitation range of 50–500,000 copies/ml
- Multiple studies have shown that HIV RNA levels predict clinical outcome
  - ◊ In general, long-term survivors have lower levels of HIV RNA (usually <10,000 copies/ml of plasma)

- ◊ Higher levels correlate with:
  - A more rapid decline in CD4 cell counts
  - More rapid progression to AIDS
  - Decreased survival
- ◊ Normal 2X–3X fluctuations in HIV RNA occur
- ◊ Therefore, sustained changes of >3X (or >0.5 log) are required to define a significant change in HIV RNA burden

- HIV Culture
  - ◊ From peripheral blood mononuclear cells (PBMCs)
    - >95% are positive in early disease
    - Quantitative load of cellular HIV rises with advanced infection
    - May help establish diagnosis of infection in newborns, infants, and high-risk adults with an indeterminate Western blot
- Using HIV blood cultures in routine management of HIV-infected persons is not recommended ($300–400 per culture at the University of Washington's Retrovirus Lab and turnaround time of 4–6 weeks)

What laboratory tests need to be obtained for a pregnant woman with HIV?

► CBC with differential and platelet count

► T-cell subsets

► Quantitative HIV RNA, "viral load"

► If not done as part of their routine prenatal care, then also draw:

- RPR
- Toxoplasmosis IgG
- CMV IgG
- ALT, AST
- Hepatitis A IgG
- Hepatitis B s Ag and core Ab
- Hepatitis C IgG
- Rubella IgG
- Herpes simplex virus (HSV) Western blot or EIA(for HSV 1 and 2 IgG)

► In addition, women newly diagnosed with HIV during pregnancy should have a repeat EIA and HIV Western blot to confirm the diagnosis.

Which laboratory tests measure the HIV disease progression?

► T-cell subsets

► Quantitative HIV RNA (measures amount of virus in the blood)

What laboratory tests are to be drawn before deciding on treatment for the HIV-infected pregnant woman?

Lab Schedule for HIV-Infected Pregnant Women

*CBC with differential and platelets may need to be drawn with T-cell subsets; check with your lab for test requirements.
**If patient is on Nevirapine, liver function tests should be monitored at 2 weeks, (prior to dose escalation), 4 weeks, 6 weeks and 8 weeks after starting treatment.

		After Treatment Began		
	Prior to Treatment	*@ 1 month*	*Monthly thereafter to evaluate for toxicity*	*Every 2-3 months during pregnancy*
CBC with differential and platelets	√	√	√	
T-cell subsets	√	√		√*
Quantitative HIV RNA	√	√		√
ALT, AST**	√	√	√	
Creatinine	√	√	√	

Please consult HIV/AIDS Treatment guidelines for details (www.hivatis.org).

CDC Classification of Disease and Reporting

What are the CDC HIV classifications of disease?

	Category A	*Category B*	*Category C*
CD4 Count	*Asymptomatic (Previous Class I, II, III*)*	*Symptomatic (Previous Class IV*) Non-AIDs*	*Symptomatic (Previous Class IV*) AIDs*
≥500 and/or 28%	A1	B1	C1
200-499 and/or 14-28%	A2	B2	C2
<200 and/or <14%	A3	B3	C3

* 1987 CDC Classifications

Symptomatic Non-AIDS
(B1, B2)

AIDS
(A3, B3 = Immunological AIDs) (C1, C2, C3 = Clinical AIDs)

Category B Symptoms
Any which the health care provider feels are HIV-related and which are NOT included in the list of Category C Symptoms.

Category C Symptoms

Candidiasis:
— Bronchi, trachea, or lungs
— Esophageal
Cervical cancer, invasive
Coccidioidomycosis, disseminated or extrapulmonary
Cryptococcosis, extrapulmonary
Cryptosporidiosis, chronic intestinal
Cytomegalovirus disease (other than liver, spleen, or nodes)
Cytomegalovirus retinitis (with loss of vision)
Herpes simplex chronic ulcers; or bronchitis, pneumonitis, or esophagitis
Histoplasmosis disseminated or extrapulmonary
HIV encephalopathy
Isosporiasis, chronic intestinal
Kaposi's sarcoma
Lymphoma: — Burkitt's (or equivalent)
— Immunoblastic (or equivalent)
— Primary in brain
M. tuberculosis: — Pulmonary
— Diss. or extrapulmonary
Mycobacterium avium complex or *M. kansasii* disseminated or extrapulmonary
Mycobacterium of other or unidentified species, disseminated or extrapulmonary
Pneumocystis carinii pneumonia
Pneumonia, recurrent
(2 or more events in a 12-month period)
Progressive, multifocal leukoencephalopathy
Salmonella septicemia, recurrent
Toxoplasmosis of brain
Wasting syndrome due to HIV

REPORTING

As of September 1, 1999, asymptomatic HIV infection became reportable in Washington State. If you are a King County provider, please report HIV cases of any classification to the Public Health — Seattle and King County HIV/AIDS Epidemiology Program at (206) 296-4645. If you are a provider working outside King County, please contact your local health department or the Washington State Department of Health at 888-367-5555 or (253) 395-6731 to report HIV cases.

Medications and Treatment During Pregnancy, Labor and Delivery

What are the different medications used to treat HIV?

- Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTI)
  - Zidovudine (ZDV, AZT)*
  - Didanosine (ddI)
  - Lamivudine (3TC)
  - Stavudine (d4T)
  - Zalcitibine (ddC)
  - Abacavir (ABC)
  - Tenofovir (TDF)
- Non-nucleoside Reverse Transcriptase Inhibitors (NNRTI)
  - Nevirapine
  - Delavirdine
  - Efavirenz (possibly teratogenic; avoid in pregnancy)
- Protease Inhibitors (PI)
  - Indinavir
  - Ritonavir
  - Saquinavir
  - Nelfinavir
  - Amprenavir
  - Lopinavir

*Only drug officially FDA-approved for use in pregnancy

What are the current treatment recommendations for HIV-positive pregnant women?

► Treat HIV-positive **NON-PREGNANT** women with:

CD4 (lymphocyte) count of <350/mm^3

Current Combination Antiretroviral Therapy For HIV-Positive Non-Pregnant Women

2 Nucleoside Reverse Transcriptase Inhibitors
and
Protease Inhibitor
or
Non-Nucleoside Reverse Transcriptase Inhibitor

► Treat HIV-positive PREGNANT women:

- In general, HIV treatment during pregnancy should be offered regardless of CD4 count and viral load.
- Pregnant women with quantitative HIV RNA >1,000 should be offered combination antiretroviral therapy with at least 3 drugs because of the benefit to reducing perinatal HIV transmission (Perinatal Guidelines, 2000). Even women with a viral load <1,000 may consider comprehensive antiretroviral therapy in pregnancy.
- Zidovudine (AZT, ZDV) is the only agent shown to reduce perinatal transmission when taken as a 3-part regimen (based on ACTG study 076 data):
  - ◊ During pregnancy
  - ◊ During labor
  - ◊ Administered to the newborn for 6 weeks
- Therefore, any treatment regimen should include AZT unless the woman is intolerant of AZT or is taking d4T (competes with AZT). Consider substitution of AZT for d4T.
- If resistant to AZT, consider including in regimen as 4th agent because it may still contribute to reducing perinatal HIV transmission even though it is unlikely to be active for maternal health.
- If possible, avoid the combination of ddI in pregnancy, as there have been case reports of fulminant lactic acidosis and death in the third trimester among women taking this nucleoside combination.

Therapy for HIV-Positive Pregnant Women

Zidovudine AZT, ZDV
200 mg. PO tid Or 300 mg PO bid
started at 12 weeks of pregnancy or later.
If possible, include ZDV in combination antiretroviral therapy
for any pregnant woman with quantitative HIV RNA >1,000

- Efavirenz is contraindicated in pregnancy due to significant teratogenicity in animal studies

► HIV-positive women who become pregnant while on antiretroviral therapy

- Regimen before pregnancy should be continued
- If the woman is taking Efavirenz, switch to another drug and counsel the woman about potential effects to fetus
- Risk of viral rebound and developing viral resistance, potentially increasing transmission or causing disease progression, must be balanced against uncertain risks of drug toxicity and teratogenicity in pregnancy
- If therapy is stopped in the first trimester, all drugs should be stopped and restarted simultaneously, or there may be an increased risk of the virus developing resistance to the drugs. Discourage stopping therapy because of the risk of viral rebound.

► Prevention of opportunistic infections during pregnancy

- All pregnant women with a CD4 count <200 should receive Pneumocystis carinii pneumonia (PCP) prophylaxis with TMP-SMX, 1 DS or 1 SS PO qd or Dapsone, 100 mg PO qd

Are there any concerns about treating pregnant women with the same medications that are used to treat HIV-infected men and non-pregnant women?

► The most studied drug for use in pregnancy is zidovudine (AZT, ZDV), which thus far has not been associated with birth defects or increased risk of adverse outcomes

► Data for uninfected infants from ACTG 076 followed from birth to a median age of 4.2 years have not indicated any differences in growth, neurodevelopment, or immunologic status among infants born to mothers who received AZT compared to those who received placebo. No malignancies have been found with short-term follow-up of up to 6 years (Culnane et al., 1999; Hanson, 1999).

► Accumulating data shows that use of Lamivudine (3TC), Stavudine (d4T), and Didanosine (ddI) in pregnancy appears to be safe for fetuses (Perinatal Guidelines, 2002)

► However, the combination of ddI and d4T over prolonged periods of time may be associated with maternal lactic acidosis in late pregnancy. For this reason, ddI/d4T should be avoided. Expert consultation is recommended.

► Mitochondrial toxicity associated with NRTI use was reported in 8 infants in France. After a large database evaluation in the U.S., no association between these findings and in utero exposure to antiretroviral drugs has been found. In additional studies, no increased risk of neurologic events has been observed (Morris, 1999).

► Limited studies of NNRTIs show that Nevirapine appears safe. Efavirenz may be associated with birth defects in animal studies and should be avoided in pregnancy (Guay et al., 1999; Perinatal Guidelines, 2000).

► Protease inhibitor (PI) use in pregnancy appears safe:

- Both pregnancy and PI therapy increase the risk of hyperglycemia; clinicians need to be aware of this potential complication and closely monitor glucose levels during pregnancy (Dube, 1998).
- Preliminary analyses of multiple Pediatric AIDS Clinical Trials Group perinatal trials and cohort studies do not indicate an elevated risk of premature delivery among infants born to women receiving combination antiretroviral therapy with or without PIs compared to those receiving single drug or no antiretroviral therapy (Brocklehurst & French, 1998).
- Adverse effects of Indinavir in non-pregnant individuals include kidney stones and hyperbilirubinemia. Hypothetical concern for development of renal stones or neonatal jaundice in the exposed fetus has not

been observed (Brocklehurst & French, 1998).

- Indinavir and Saquinavir should be given with Ritonavir in pregnancy to ensure that drug levels are adequate.

► **The Antiretroviral Pregnancy Registry** is an epidemiologic project to collect observational data on antiretroviral exposure during pregnancy with the intention of defining risks for antiretroviral therapy. The registry is maintained by antiretroviral manufacturers and the CDC. Send anonymous prospective reports of HIV-infected pregnant women who are receiving antiretrovirals to:

Registrar
Antiretroviral Pregnancy Registry
115 North 3rd Street, Suite 306
Wilmington, NC 28401
Phone:1-800-258-4263 FAX: 1-800-800-1052

► Because of the complexities of antiretroviral therapy and rapidly changing information about HIV medications in pregnancy, consultation with an infectious disease specialist knowledgeable about HIV and pregnancy is strongly recommended.

History and Physical

Should there be added routines in the history and physical exam of the HIV-positive pregnant woman?

► History

- A woman who tests HIV positive in pregnancy should be asked about previous deliveries. She should be encouraged to have her other children tested for HIV, unless she was known to be HIV negative throughout those pregnancies.
- At every visit, the health care provider should inquire about constitutional signs and symptoms:
  - ◊ Fevers
  - ◊ Night sweats
  - ◊ Respiratory problems
  - ◊ Nausea/vomiting
  - ◊ Diarrhea

► Physical exam

- At least once each trimester, the patient's mouth should be inspected for thrush and oral hairy leukoplakia
- All lymph nodes should be palpated, since a swollen, tender lymph node may be a harbinger of a more serious infection or malignancy
- Abdomen should be palpated for liver/spleen enlargement
- Skin should be observed for rash, seborrheic dermatitis
- Neurologic exam, including DTRs, for neuropathies
- For women newly diagnosed with HIV:

◊ Do a Pap smear

– If normal, repeat every 6 months x 2, then annually

– If abnormal, refer for colposcopy and directed biopsy

◊ If CD4 count <100/mm^3, refer to an ophthalmologist for baseline funduscopic exam to rule out CMV retinitis

Medication During Labor

What medications should be used for the HIV-positive pregnant woman in labor?*

► The standard of care for HIV-positive pregnant women who have current or prior experience with antiretroviral therapy is as follows:

- Administer intravenous Zidovudine (AZT, ZDV) to the pregnant woman in labor at the following doses:

◊ On admission to labor and delivery, give:

IV AZT 2 mg/kg over 1 hour as a loading dose

◊ Once the loading dose is completed, administer:

Continuous IV infusion of 1 mg/kg/hour throughout labor

- If scheduled cesarean delivery is planned, provide at least 2–4 hours of IV AZT before delivery
- Stop IV AZT after the umbilical cord has been cut
- If the pregnant woman is currently taking antiretrovirals in addition to AZT, administer those drugs by mouth during labor

- For the standard of care for infants born to HIV-positive women, see page 33

► There are now 4 effective antiretroviral therapy options available for HIV-infected pregnant women presenting in labor without a history of prior antiretroviral therapy and for their newborn infants (new recommendations from U.S. Public Service Task Force for Use of Antiretroviral Drugs in Pregnant Women Infected with HIV-1 Virus for Maternal Health and for Reducing Perinatal HIV-1 Transmission in the U.S., August, 2002).

The following is the most recommended regimen for women in the U.S.:

Mother: Same AZT regimen as in box above
and
Newborn: AZT 2 mg/kg PO q 6 hrs for 6 weeks

*If the woman does not have a documented history of a test for HIV during the current pregnancy, a rapid test for HIV such as OraQuick should be strongly considered at the time of labor or delivery.

The following treatments are alternatives but could lead to maternal antiretroviral resistance and are generally not used in the U.S.

Mother: Nevirapine single 200 mg PO dose at onset of labor
and
Newborn: Nevirapine single 2 mg/kg PO dose at age 48–72 hours*

OR

Mother: AZT 600 mg PO at onset of labor,
followed by 300 mg PO q 3 hrs until delivery
and
Mother: 3TC 150 mg PO at onset of labor,
followed by 150 mg PO q 12 hrs until delivery
and
Newborn: AZT 4 mg/kg PO q 12 hrs
and
Newborn: 3TC 2 mg/kg PO q 12 hrs for 7 days

OR

Mother: AZT 2 mg/kg IV bolus, followed by
continuous infusion of 1 mg/kg/hr until delivery
and
Mother: Nevirapine single 200 mg PO dose at onset of labor
and
Newborn: AZT 2 mg/kg PO every 6 hrs for 6 weeks
and
Newborn: Nevirapine single 2 mg/kg PO dose at age 48–72 hrs

Note: For an update of HIV treatment guidelines for pregnant women, go to the following website: www.aidsinfo.nih.gov

Information about HIV medications for pregnant and postpartum women and newborns outdates quickly. For current recommendations, contact

- ► An infectious disease specialist knowledgeable about perinatal HIV
- ► Go to http://www.aidsinfo.nih.gov/
- ► Call the CDC Hotline 1-800-342-AIDS
- ► Call Northwest Family Center 206-731-5100

*If the mother received Nevirapine <1 hour prior to delivery, the infant should be given 2 mg./kg oral Nevirapine as soon as possible after birth and again at 48-72 hours.

Cesarean Birth

Does a cesarean birth decrease the risk of infant infection?

Early studies indicate there is a significant relationship between the mode of delivery and vertical transmission of HIV. This body of evidence, accumulated mostly before the use of HAART and without any data regarding maternal viral load, indicates that scheduled cesarean delivery (performed before the onset of labor and/or rupture of membranes) reduces the risk of vertical transmission of HIV compared with either unscheduled cesarean or vaginal deliveries. This finding holds true whether or not the woman is receiving AZT therapy. Whether cesarean delivery offers any benefit to women on HAART or to women with a low or undetectable viral load is unknown.

Maternal morbidity is greater with cesarean delivery than with vaginal delivery in HIV-infected women, especially among women who have a low CD4 count (ACOG Committee Opinion, 2000; Grubert et al., 1999; Stringer et al., 1999; The European Mode of Delivery Collaboration, 1999; The International Perinatal HIV Group, 1999).

Although many issues remain unresolved because of insufficient data, the American College of Obstetricians and Gynecologists (ACOG Bulletin #234, May 2000) makes the following recommendations:

- ► HIV-infected pregnant women should be appropriately counseled regarding
  - Risk of vertical transmission:
    - ◊ Probability of transmission from an untreated mother to fetus/infant is about 25%
    - ◊ With AZT treatment, risk of transmission is reduced to 5–8%
    - ◊ With highly active antiretroviral treatment (HAART) consisting of 3 or more drugs, and suppression of plasma HIV to a low level (viral load <1,000 copies /ml), transmission is reduced to about 2%
    - ◊ Without HAART, or with a viral load >1,000 copies, ZDV plus a scheduled cesarean delivery at 38 weeks gestation can also reduce the risk of transmission to about 2%
    - ◊ No combination of therapies and/or scheduled cesarean delivery can guarantee that a newborn will not become infected
  - Maternal risks associated with cesarean delivery for HIV-infected women:
    - ◊ Postoperative fever
    - ◊ Endometritis
    - ◊ Wound infection
    - ◊ Urinary tract infection
- ► Scheduled cesarean delivery should be offered to women with a viral load >1,000 copies/ml, whether or not they are taking antiretroviral therapy
- ► Risks of cesarean delivery—which are greater for the mother—must be balanced with the benefits expected for the neonate, and the choice of delivery must be individualized
- ► The woman's autonomy should be respected in making her own informed decision regarding route of delivery

Avoiding Risk of Transmission

What can be done in labor to minimize the risk of newborn infection?

Intravenous AZT and/or other drugs as recommended by the U.S. Public Service Task Force for Use of Antiretroviral Drugs in Pregnant Women Infected with HIV-1 Virus for Maternal Health and for Reducing Perinatal HIV-1 Transmission in the U.S. (see page 28). Whenever possible:

AVOID

- ► Amniocentesis
- ► Fetal scalp electrode and intrauterine pressure catheter (IUPC)
- ► Forceps and vacuum extractor
- ► Artificial rupture of membranes
  - Studies show an increased risk of infection with rupture of membranes over 4 hours
  - If membranes rupture before labor, begin oxytocin augmentation as soon as possible
- ► Episiotomy, if possible

What can be done to try to minimize infection in the newborn immediately after birth?

- ► At birth, avoid vigorous suctioning of the mouth and nose
- ► Handle the newborn carefully to avoid trauma
- ► Wash the newborn with soap (per hospital procedure) before giving injections or drawing blood
- ► Start oral AZT within the first 6–12 hours, ideally after the first infant blood draw, or start other regimen according to new guidelines (see page 28-29)

Postpartum Management

Should the woman continue to be treated after delivery?

It depends on her health, current drug regimen, and HIV disease status

- ► If a woman is on AZT only for prevention of perinatal HIV transmission, therapy should be stopped at delivery
- ► If a woman is receiving highly active antiretroviral therapy (HAART), indications for continued treatment after delivery should be evaluated.
  - Women with a baseline CD4 count >350 prior to therapy do not have strong clinical indications to continue treatment after delivery
  - If a woman has indications for ongoing antiretroviral treatment after delivery, the provider should help her develop strategies that will promote adherence to her regimen during the postpartum period
  - All women should have a repeat CD4 count and viral load 6 weeks after delivery and then approximately every 3-4 months thereafter, regardless of whether they stay on antiretroviral therapy.

What is the postpartum care for an HIV-infected woman?

- ► Advise not to breastfeed
  - Transmission of HIV via breast milk has been well documented
- ► Give routine postpartum care, including contraception
  - Provide family planning education, method, or referral services
- ► Assess needs for psychological support
  - Address maternal fears of infant infection
  - Provide support services as needed (e.g., case management, mental health services)

What contraception should be used for the HIV-positive woman?

- ► Condoms are always recommended, even if her partner is HIV-positive
- ► Hormonal
  - Depo-provera
  - Oral contraceptives (OCs)
    - ◊ Must consider concomitant medications for effects on metabolism, toxicity, and efficacy
    - ◊ Two drugs used for mycobacterium avian complex (MAC) prophylaxis decrease efficacy of oral contraceptives:
      - – Rifabutin (Mycobutin)
      - – Rifampin (Rimactane, Rifadin)
    - ◊ These antiretroviral drugs may decrease the efficacy of oral contraceptives:
      - – Nevirapine
      - – Nelfinavir
      - – Ritonavir
      - – Efavirenz
      - – Amprenavir
  - Lunelle (a.k.a. Cyclofem, Cyclo-provera) is a once-a-month, injectable combination of DMPA + estradiol cypionate.
  - A transdermal patch containing ethinyl estradiol and norelgestromin
  - A vaginal ring containing ethinyl estradiol and Etonorgestrel
    - ◊ Lunelle, the transdermal patch, and the vaginal ring may have decreased efficacy with some antiretroviral drugs (see list above).
- ► Diaphragm with spermicide
- ► IUD can be considered for a monogamous couple who is not at high-risk of acquiring other STDs. Levonorgestrel IUD (Mirena) may be the IUD of choice for HIV positive women because the progesterone in this IUD may decrease menstrual blood volume.
- ► Provide emergency contraception information and supply.

What education should be provided to the HIV-infected woman before she is discharged from the hospital?

DO

- ► Encourage the HIV-positive woman to hold, hug, and kiss her baby
  - She does not need to wear gloves to touch her baby or change diapers
  - Stress good hand washing
- ► Encourage friends and family to hold the baby
  - An infected baby will not transmit the virus by holding or hugging
- ► Instruct the mother to continue giving her baby oral AZT syrup every 6 hours for the first 6 weeks of life, or other regimen according to clinician

DO NOT

- ► Breastfeed
- ► Bite off the baby's fingernails or toenails
- ► Pre-chew food for infant
- ► Hold the baby's pacifier in the mother's mouth
- ► Share a toothbrush with anyone, especially children
- ► Touch exudate from an infected person's lesion, as this exudate contains HIV

The HIV-Exposed Infant

What laboratory tests should be done on the HIV-exposed newborn, ideally within the first 24 hours of life?

- ► CBC with differential and platelets
- ► ALT/AST
- ► HIV DNA PCR to test for viral infection
  - Do **not** use cord blood because of potential maternal contamination leading to a false positive result .

Note: *Maternal zidovudine (AZT, ZDV) use can cause anemia and elevated liver enzymes in the newborn. Repeat measurement of hemoglobin and ALT/AST at 4-6 weeks of age.*

Data are limited concerning potential toxicities in infants whose mothers received HAART. More intensive monitoring of hematologic and serum chemistry during the first few weeks of life is advised in these infants.

Are HIV-exposed neonates treated with any medications?

► On the basis of ACTG 076 study, neonates are treated with:

> Zidovudine syrup 2 mg/kg/dose PO every 6 hours (for a total of 8 mg/kg/day) for the first 6 weeks of life

► If the neonate cannot take zidovudine orally and needs IV treatment:

> 1.5 mg/kg/dose IV every 6 hours, for a total of 6 mg/kg/day

► Ideally, infant labs are drawn before starting zidovudine; however, the goal is to start the drug within the first 6–12 hours of life, even if labs have not been drawn.

► See pages 28-29 for new antiretroviral treatment options for infants born to mothers who have received no antiretroviral therapy prior to labor. Treatment for the infant would depend on what treatment the mother received during labor.

► For infants born to mothers who have received no antiretroviral therapy during pregnancy or intrapartum, the 6-week neonatal zidovudine regimen as described above should be initiated as soon as possible after delivery. Consultation with an HIV specialist is highly recommended.

► (Correction 8/11/03) The current pediatric standard of care is to begin all HIV-exposed infants on Pneumocystis carinii pneumonia (PCP) prophylaxis with TMP-SMX 150 (TMP) mg/m^2 in divided doses 2X/day, 3 days/week beginning at 4–6 weeks of age and continuing until two definitive HIV-negative tests are obtained, one of which is drawn after one month of age and the other draw after 4 months of age.

What are the options for follow-up testing of the HIV-exposed infant?

For testing and consultation, refer to

Northwest Family Center (NWFC)
Harborview Medical Center, Seattle
206-731-5100 (clinic) or
206-731-3066 (case management)
1-800-462-4965

Pediatric Infectious Disease Group
Children's Hospital and Regional Medical Center, Seattle
206-987-2073

Local State and County Health Departments or Community Clinics (see Appendix B)

What is the schedule for HIV testing of the infant born to an HIV-positive mother?

For early diagnosis, specific viral tests should be done on a regular basis.

Lab Schedule for Infants Born to an HIV-Positive Mother

	12-48 hrs of life	1-2 wks	4-8 wks	4 mos	6 mos	18 mos
HIV DNA PCR	√	√	√	√	√	
HIV serology (EIA and Western blot)						√

How is HIV infection diagnosed in a child <18 months of age who is known to be born to an HIV-positive mother?

► A child <18 months is tested by using specific viral HIV detection tests. These tests include:

- HIV DNA PCR
- HIV culture
- Quantitative HIV RNA may be used, but this test is not approved as an HIV diagnostic test and results should be interpreted with assistance of an HIV specialist

► A child is infected if there are two separate positive specific viral HIV detection tests from two different dates excluding cord-blood.

► A child is not infected under age 18 months if there are two negative tests, one at least over one month of age and the other over four months.

► A positive HIV antibody test (serology) indicates exposure but not HIV infection in child <18 months because:

- Passive transfer of maternal antibody from the pregnant woman to her fetus occurs during pregnancy
- A child under 18 months of age is expected to be antibody positive for HIV, reflecting maternal antibody

► By 18 months of age the maternal HIV antibody should be gone, so an antibody test is appropriate for screening

Appendix A: Resource Directory

Northwest Family Center (206) 731-5100 (clinic) or
Harborview Medical Center 1-800-462-4965
325 - 9th Avenue
Seattle, WA 98102

- Obstetric, gynecologic, and medical care and case management for HIV-infected women and children
- Consultation on managment of HIV-infected pregnant women
- AIDS Clinical Trial Group (ACTG) clinical trials for HIV-positive pregnant women

BABES Network
1001Broadway, Suite 100 (206) 720-5566
Seattle, WA 98122 1-888-292-1912
the_staff@babesnetwork.org

Children's Hospital and Regional Medical Center
Pediatric Infectious Disease Group (206) 987-2073
4800 Sandpoint Way N.E., CH-32
Seattle, WA 98105

- Information and medical care for HIV-infected and exposed children
- ACTG clinical trials for HIV-positive children

All Washington State Health Departments (See Appendix B)

- HIV and STD information, testing, and counseling referrals
- Partner notification
- HIV/AIDS reporting

Public Health (Seattle & King County) (206) 296-4649 (main no.)
HIV/AIDS Program www.metrokc.gov/health/apu
400 Yesler Way, 3rd floor
Seattle, WA 98104

- HIV/AIDS Epidemiology (206) 296-4645
  - For health care providers in King County to report HIV/AIDS cases
- Partner Notification Services (206) 205-7192
  - For health care providers in King County
- HIV/AIDS and STD Hotline (206) 205-7837
  - For information and testing referrals

  Outside Seattle 1-800-272-AIDS
  In Seattle 1-800-678-1595

Alcohol/Drug Hotline (24-hour) 1-800-562-1240

- Provides statewide referral information about treatment, counseling, and support services by county/city for teens and adults

Washington State Department of Health 1-800-272-2437
HIV/AIDS Prevention and Education Service
P.O. Box 47840
Olympia, WA 98504-7840

- Waiting room pamphlets for health care provider offices
- Literature requests
- Referrals to other state offices and resources

Northwest AIDS Education & Training Center (206) 221-4944
Cabrini Medical Tower
901 Boren Avenue, Suite 1100
Seattle, WA 98104-3508

- Clinical training and educational support for health care professionals

AIDS Clinical Trials Unit (206) 731-3184

- HIV/AIDS ACTG clinical trials and treatment for adult residents (age 13 and over) of Washington State

AIDS Information—Guidelines, Drugs, Vaccines and Clinical Trials 1-800-874-2572

- National information hotline for clinical trials
- ATIS and AIDS Clinical Trials Information Services have been merged into www.aidsinfo.nih.gov
- A service of DHHS
- Central resource for federally-approved treatment guidelines for HIV & AIDS

CDC HIV/AIDS Hotline (24-hour) 1-800-342-AIDS

- Information on HIV issues www.cdc.gov/epo/mmwn/mmwr.html
- Ordering client or professional education materials

Family Resource Guide for HIV-Affected Families 1-800-272-2437

- Developed by Children's Hospital and Regional Medical Center, WA State Department of Health, and Babes
- Contains list of statewide health and social service resources for children and families affected by HIV

Starting Point: Resources for Children with Special Health Care Needs in Washington State (206) 987-5709 (ext. 1) to order copies

- ► Developed by Children's Hospital and Regional Medical Center, WA State Department of Health, and Healthy Mothers, Healthy Babies Program
- ► Family Resource Guide with list of statewide health and social service resources for children and families

American College of Obstetricians and Gynecologists (ACOG) (202) 638-5577 www.acog.org

- ► Patient educational materials on HIV testing and pregnancy

POCAAN

Seattle (Main Office)
2200 Rainier Ave. S.
Seattle, WA 98144
(206) 322-7061
(206) 322-7204 fax
www.pocaan.org

Tacoma
919 South 9th Street
Tacoma, WA 98405
(253) 272-2577
(253) 272-2709 fax

Yakima
15 N. Naches Avenue
Yakima, WA 98901
(509) 249-8725
(509) 249-8736 fax

Washington State HIV/AIDS Hotline 1-800-272-2437

Lifelong AIDS Alliance
1002 East Seneca
Seattle, WA 98122
(206) 328-8979 (Main)
(206) 957-1717 (access line)
(206) 325-2689 fax
www.lifelongaidsalliance.org
TDD (206) 323-2685

Dolores Braun (206) 615-2290; 1-800-362-1710

U.S. Office of Civil Rights
Region X: 2201 - 6th Avenue (MS: RX-11)
Seattle, WA 98121

Appendix B: Washington State Local Health Ju-

Adams County Health Department
108 West Main
Ritzville, WA 99169-1407
(509) 659-3319

Asotin County Health District
431 Elm Street
Clarkston, WA 99403
(509) 758-3344

Benton-Franklin Health District
471 Williams Blvd.
Richland, WA 99352-3520
(509) 943-2614 (Richland)
(509) 547-9737 (Pasco)
(509) 586-0207 (Kennewick)

Chelan-Douglas Co. Health District
200 Valley Mall Parkway
East Wenatchee, WA 98802
(509) 886-6400; 1-800-336-5306

Clallam County Health Department
223 East 4th Street
Port Angeles, WA 98362-3098
(360) 417-2352

Clark County Health Department
2000 Ft. Vancouver Way
Vancouver, WA 98663
(360) 397-8089

Columbia County Public Health District
221 East Washington St., #101 PH
Dayton, WA 99328
(509) 382-2181
Cowlitz County Health Department
1952 Ninth Avenue
Longview, WA 98632-4045
(360) 414-5599

Garfield County Health District
10th & Columbia (P.O. Box 130)
Pomeroy, WA 99347
(509) 843-3412

Grant County Health District
1021 West Broadway
Moses Lake, WA 98837
(509) 766-7960

Grays Harbor County Health Department
2109 Sumner Avenue
Aberdeen, WA 98520
(360) 532-8631

Island County Health Department
410 North Main (P.O. Box 5000)
Coupeville, WA 98239-5000
(360) 679-7351

Jefferson County Health Deparment
Castle Hill Center
615 Sheridan Street
Port Townsend, WA 98368-2439
(360) 385-9400

Kitsap County Health Dept.
109 Austin Drive
Bremerton, WA 98312
(360) 337-5235; 1-800-874-2437
Kittitas County Health Department
507 Nanum Street
Ellensburg, WA 98926
(509) 962-7515

Klickitat County Health Department
228 West Main Street
MS: CH14
Goldendale, WA 98620
(509) 773-4565

Lewis County Health Department
Health Services Building
360 N.W. North Street
Chehalis, WA 98532-1900
(360) 740-1368; 1-800-562-6130 (X-1368)

Lincoln County Health Department
90 Nichols Street (P.O. Box 1207)
Davenport, WA 99122
(509) 725-1001

Mason County Health Department
303 North 4th
Shelton, WA 98584
(360) 427-9670, X-400

NE Tri-County Health District
240 East Dominion (P.O. Box 270)
Colville, WA 99114
(509) 684-5048

Okanogan County Health District
1234 South 2nd Avenue
Administration Building
Okanogan, WA 98840
(509) 422-7140

Pacific County Health Department
1216 West Robert Bush Drive
P.O. Box 26
South Bend, WA 98586
(360) 875-9343

San Juan County Health Department
145 Rhone Street (P.O. Box 607)
Friday Harbor, WA 98250-0607
(360) 378-4474

Seattle—King County–Public Health
HIV/AIDS Program
400 Yesler Way, 3rd floor
Seattle, WA 98104
(206) 296-4649
HIV/STD Hotline: 1-800-678-1595

Skagit County Health Department
Courthouse Administration Building
700 South 2nd Street, Room 301
Mt. Vernon, WA 98273-3864
(360) 336-9380

Skamania County Health Department
683 SW Rock Creek Drive
Stevenson, WA 98648
(509) 427-5138

Snohomish Health District
3020 Rucker Avenue, #206
Everett, WA 98201-3971
(425) 339-5251; 1-800-344-2437

Spokane Regional Heath District
1101 West College Avenue
Spokane, WA 99201-2095
(509) 324-1600; 1-800-456-3236

Tacoma/Pierce County Health Department
3629 South "D" Street, CHD-059
Tacoma, WA 98408-6897
(253) 798-6060

Thurston County Health Department
412 Lilly Road NE
Olympia, WA 98506-5132
(360) 786-5581 (press 3 at main menu)

Wahkiakum Health Department
64 Main Street
Cathlamet, WA 98612
(360) 795-6207

Walla Walla County/City Health Department
310 West Poplar (P.O. Box 1753)
Walla Walla, WA 99362-0346
(509) 527-3290
Whatcom County Health Department
509 Girard Street
Bellingham, WA 98227-0935
(360) 676-4593

Whitman County Health Department
Public Services Building
North 310 Main Street
Colfax, WA 99111
(509) 397-6280

Yakima County Health District
104 North First Street
Yakima, WA 98901-2267
(509) 249-6518; 1-800-535-2271

Appendix C: Free Regional and National Telephone Consultation

Medcon (24 hours) (206) 543-5300, or
1-800-326-5300

- University of Washington medical consultation
- For medical providers in Washington, Alaska, Montana, and Idaho, linking providers with medical school faculty

Warmline 1-800-933-3413
http://www.ucsf.edu/hivcntr

- National HIV telephone consultation service for health care providers
- 7:30 am to 5:00 pm PST, Monday through Friday (voice mail available 24-hours/day, 7days/week)

Pepline 1-888-HIV-4911
http://www.ucsf.edu/hivcntr

- National clinicians' post-exposure prophylaxis hotline

National AIDS Hotlines 1-800-342-AIDS (English)
1-800-344-SIDA (Spanish
1-800-AIDS-TTY (Deaf/Hearing Impaired)

National STD Hotline 1-800-227-8922
1-800-243-7889 TDD

National AIDS Information Clearinghouse 1-800-458-5231

Appendix D: Websites

HIV/AIDS Treatment Information Service (ATIS)
www.aidsinfo.nih.gov

- Central resource for federally-approved treatment guidelines for HIV & AIDS

AIDS Education Global Information Service (AEGIS)
www.aegis.com

- HIV daily briefing, updated hourly

Johns Hopkins AIDS Service
www.hopkins-aids.edu

- Expert Q&A, publications, medical education, resources, managed care, epidemiology, prevention, treatment

Medscape (Infectious Diseases)
http:/ID.medscape.com/Home/Topics/ID/InfectiousDiseases.html

HIV InSite (sponsored by UCSF)
http://hivinsite.ucsf.edu/

- Medical information, prevention and education, social issues and policy, statistics and epidemiology

Northwest AIDS ETC
http://depts.washington.edu/nwaetc/

- What's new, courses and services, provider resources, associated centers

HIV/AIDS Bureau
United States Department of Health and Human Services
Health Resources and Services Administration
www.hab.hrsa.gov

References

ACOG Committee Opinion. Scheduled cesarean section delivery and the prevention of vertical transmission of HIV infection. May 2000;234:1–5.

ACOG Statement of Policy. Joint statement of ACOG/AAP on human immunodeficiency virus screening. May 1999:1–2.

Boyer PJ, Dillon M, Navaie M, et al. Factors predictive of maternal-fetal transmission of HIV-1. *Journal of American Medical Association* 1994;271:1925-1930.

Brocklehurst P, French R. The association between maternal HIV infection and perinatal outcome: a systematic review of the literature and meta-analysis. *British Journal of Obstetrics and Gynaecology* 1998;105:836–848.

Celum CL, Coombs RW, Lafferty W, et al. Indeterminate human immunodeficiency virus type 1 Western blot: Seroconversion risk, specificity of supplemental tests, and an algorithm for evaluation. *Journal of Infectious Diseases* 1991;164(4):656-64.

Centers for Disease Control and Prevention. U.S. Public Health Service Task Force recommendations for the use of antiretroviral drugs in pregnant women infected with HIV-1 for maternal health and for reducing perinatal HIV-1 transmission in the United States. *Morbidity and Mortality Weekly Report* 1998; 47:1-30.

Centers for Disease Control and Prevention. U.S. Public Health Service Task Force guidelines for the use of antiretroviral agents in pediatric HIV infections. *Morbidity and Mortality Weekly Report* 1998;47(RR-04).

Centers for Disease Control and Prevention. U.S. Public Health Service Task Force revised guidelines for performing CD4+ T-Cell determinations in persons infected with human immunodeficiency virus. *Morbidity and Mortality Weekly Report* 1997;46(RR-2):1-29.

Centers for Disease Control and Prevention. U.S. Public Health Service recommendations for human immunodeficiency virus counseling and voluntary testing for pregnant women. *Morbidity and Mortality Weekly Report* 1995; 44:1-15.

Centers for Disease Control and Prevention. U.S. Public Health Service IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus. A summary. *Morbidity and Mortality Weekly Report* 1995;44(RR-8):1-34.

Connor EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. *New England Journal of Medicine* 1994;331:1173-1180.

Culnane M, Fowler MG, Lee SS, et al. Lack of long-term effects of in utero exposure to zidovudine among uninfected children born to HIV-infected women. *JAMA* 1999;281:151–157.

Department of Health and Human Services. Guidelines for the use of antiretro-viral agents in HIV-infected adults and adolescents. January 28, 2000.

Dube M. Metabolic complications of antiretroviral therapies. AIDS Clinical Care 1998;10:41–48.

Duliege AM, Amos CI, Felton S, et al. Birth order, delivery route and concordance in the transmission of human immunodeficiency virus type 1 from mothers to twins. International Registry of HIV-Exposed Twins. *Journal of Pediatrics* 1995;126:625-632.

Dunn DT, Newell ML, Mayoux MJ, et al. Mode of delivery and vertical transmission of HIV-1: A review of prospective studies. *Journal of Acquired Immune Deficiency Syndrome* 1994;7:1064-1066.

Eastman PS, Shapiro DE, Coombs RW, et al. Maternal viral genotypic zidovudine resistance and infrequent failure of zidovudine therapy to prevent perinatal transmission of human immunodeficiency virus type 1 in Pediatric AIDS Clinical Trial Group Protocol 076. *Journal of Infectious Disease* 1998;177:557–564.

Elliot V. Routine prenatal care should include HIV screening. American Medical News 2000;43:19. *Lancet* 1999;354:795–802.

European Collaborative Study: Perinatal findings in children born to HIV-infected mothers. *British Journal of Obstetrics and Gynecology* 1994; 101:136-141.

European Collaborative Study: Cesarean section and risk of vertical transmission of HIV-infection. *Lancet* 1994;343:1464-1467.

European Collaborative Study: Risk factors for mother-to-child transmission of HIV-1. *Lancet* 1992;339:1007-1012.

FDA Public Health Advisory: Reports of diabetes and hyperglycemia in patients receiving protease inhibitiors for the treatment of human immunodeficiency virus (HIV). *JAMA* 1997;278:379.

Garcia PM, Kalish LA, Pitt J, et al. Maternal levels of human immunodeficiency virus type 1 RNA and the risk of perinatal transmission.
New England Journal of Medicine 1999;341:394–402.

Grubert TA, Reindell D, Kastner R, et al. Complications after caesarean section in HIV-1 infected women not taking antiretroviral treatment. *Lancet* 1999;354:1612–3.

Guay L, Musoke P, Fleming T, et al. Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: HIVNET 012 randomized trial.

Gwinn M, Papaioanou M, George JR, et al. Prevalence of HIV infection in childbearing women in the United States. *Journal of American Medical Association* 1991;265:1704-1708.

Hanson IC, Antonelli TA, Sperling RS, et al. Lack of tumors in infants with perinatal HIV-1 exposure and fetal/neonatal exposure to zidovudine. *Journal of Acquired Immunodeficiency Syndrome* 1999; 20:463–467.

Hitti J, Watts DH, Burchett SK, et al. Herpes simplex virus seropositivity and reactivation in labor among pregnant women infected with human immunodeficiency virus-1. *American Journal of Obstetrics and Gynecology* 1997;177(2):450-454.

Institute of Medicine. Committee on Perinatal Transmission of HIV. Reducing the odds: Preventing perinatal transmission of HIV in the United States. National Academy Press 1999:1–20.

Jackson JB, MacDonald KL, Cadwell J, et al. Absence of HIV infection in blood donors with indeterminate Western blot tests for antibody to HIV-1. *New England Journal of Medicine* 1990;322(4):217-222.

Kass N, Taylor H, Anderson J. Treatment of human immunodeficiency virus during pregnancy: The shift away from an exclusive focus on fetal protection to a more balanced approach. *American Journal of Obstetrics & Gynecology* 2000;182:856–859.

Kaunitz AM, Mishell DR Jr. Lunelle monthly contraceptive injection (medroxy- progesterone acetate and estradiol cyprionate injectable suspension): a contraceptive method for women in the U.S. and worldwide. *Contraception* 1999;60:177–8.

Lorenzi P, Spicher VM, Laubereau B, et al. Antiretroviral therapies in pregnancy: Maternal, fetal and neonatal effects. Swiss HIV Cohort Study, the Swiss Collaborative HIV and Pregnancy Study, and the Swiss Neonatal HIV Study. *AIDS* 1998;12:F241–247.

Matheson PB, Thomas PA, Abrams EJ, et al. Efficacy of antenatal zidovudine in reducing perinatal transmission of human immunodeficiency virus type 1 (HIV). *Journal of Infectious Disease* 1995;172:353-358.

Mayaux MJ, Blanche S, Rouzious C, et al. Maternal factors associated with perinatal HIV-1 transmission: The French cohort study: 7 years of follow-up observation. *Journal of Acquired Immune Deficiency Syndrome* 1995; 8:188-194.

McCormick M, Davidson E, Stoto M. Preventing perinatal transmission of human immunodeficiency virus in the United States. *Obstetrics & Gynecology* 1999;94:795–798.

McGowan J, Crane M, Wiznia A, Blum S. Combination antiretroviral therapy in human immunodeficiency virus-infected pregnant women. *Obstetrics & Gynecology* 1999;94:641–646.

Minkoff H, Augenbraun M. Antiretroviral therapy for pregnant women. *American Journal of Obstetrics & Gynecology* 1997;176:478–489.

Minkoff H, Burns DN, Landesman S, et al. The relationship of the duration of ruptured membranes to vertical transmission of human immunodeficiency virus. *American Journal of Obstetrics and Gynecology* 1995;173:585-589.

Mofenson LM, Lambert JS, Stiehn ER, et al. Risk factors for perinatal transmission of human immunodeficiency virus type 1 in women treated with zidovudine. *New England Journal of Medicine* 1999;341:385–393.

Morris AAM, Carr A. HIV nucleoside analogues: new adverse effects on mitochondria? *Lancet* 1999;354:1046–1047.

Nduati R, John G. Mbori-Ngacha D, et al. Effects of breastfeeding and formula feeding on transmission of HIV-1: A randomized clinical trial. *JAMA* 2000;283:1167–1174.

Paz I, Seidman DS, Mashiach S, Stevenson DK. Maternal transmission of human immunodeficiency virus type 1. *Obstetrics and Gynecological Survey* 1994;49:577-584.

Pediatric AIDS Clinical Trials Group 382, Version 2.0, May 26, 1998.

Perinatal HIV Guidelines Working Group. Revisions to the 1998 Public Health Service Task Force recommendations for the use of antiretroviral drugs in pregnant women infected with HIV-1 for maternal health and for reducing perinatal HIV-1 transmission in the United States. February 2000;1–35.

Perinatal HIV Guidelines Working Group. Recommendations for use of antiretroviral drugs in pregnant women for maternal health and intervention to reduce Perinatal HIV-1 transmission in the United States. August 30, 2002; 1-50.

Public Health Seattle & King County HIV/AIDS Epidemiology Program. HIV reporting in Washington State. September 1999:1–4.

Sperling RS, Shapiro DE, Coombs RW, et al. Maternal viral load, zidovudine treatment and the risk of transmission of human immunodeficiency virus type 1 from mother to infant. *New England Journal of Medicine* 1996; 335:1621-1629.

Spitzer M. Lower genital tract intraepithelial neoplasia in HIV-infected women: guidelines for evaluation and management. *Obstetrical and Gynecological Survey* 1999;54:131–137.

St. Louis ME, Kamenga M, Brown C, et al. Risk for perinatal HIV-1 transmission according to maternal immunologic, virologic and placental factors. *Journal of American Medical Association* 1993;269:2853-2859.

Stringer J, Rouse D, Goldenberg R. Prophylactic cesarean delivery for the prevention of perinatal human immunodeficiency virus transmission. *Journal of the American Medical Association* 1999;281:1946.

Temmerman M, Chomba EN, Ndinya-Achola J, et al. Maternal human immunodeficiency virus-1 infection and pregnancy outcome. *Obstetrics and Gynecology* 1994;83:495-501.

The European Mode of Delivery Collaboration. Elective cesarean section versus vaginal delivery in prevention of vertical HIV-1 transmission: a randomized clinical trial. *Lancet* 1999;353:1034–1039.

The International Perinatal HIV Group. The mode of delivery and the risk of vertical transmission of human immunodeficiency virus type 1: a meta-analysis of 15 prospective cohort studies. *New England Journal of Medicine* 1999;340:977–987.

U.S. Public Health Service. IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunmodeficiency virus. 1999.

VanderPerre P, Lepage P, Homsy J, et al. Mother-to-infant transmission of human immunodeficiency virus by breast milk: Presumed innocent or presumed guilty? *Clinical Infectious Disease* 1992;15:502-507.

DOH Publication 950-145; 5/2003